

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Heiko Urtel et al.

Application No.: 10/588,948

Confirmation No.: 2462

Filed: August 10, 2006

Art Unit: 1793

For: HYDROGENATION METHOD FOR
PRODUCING OPTICALLY ACTIVE
ALCOHOLS OR CARBOXYLIC ACIDS

Examiner: C. B. Nguyen

APPEAL BRIEF

MS Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

As required under § 41.37(a), this brief is filed within two months of the Notice of Appeal filed in this case on October 2, 2009, and is in furtherance of said Notice of Appeal.

The fees required under § 41.20(b)(2) are dealt with in the accompanying
TRANSMITTAL OF APPEAL BRIEF.

This brief contains items under the following headings as required by 37 C.F.R. § 41.37 and M.P.E.P. § 1205.2:

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| I. | Real Party In Interest |
| II | Related Appeals and Interferences |
| III. | Status of Claims |
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| V. | Summary of Claimed Subject Matter |
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I. REAL PARTY IN INTEREST

The real party in interest for this appeal is:

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II. RELATED APPEALS AND INTERFERENCES

There are no other appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in this appeal.

III. STATUS OF CLAIMS

A. Total Number of Claims in Application

There are 20 claims pending in application.

B. Current Status of Claims

1. Claims canceled: 6
2. Claims withdrawn from consideration but not canceled: 0
3. Claims pending: 1-5 and 7-21
4. Claims allowed: 0
5. Claims rejected: 1-5 and 7-21

C. Claims On Appeal

The claims on appeal are claims 1-5 and 7-21

IV. STATUS OF AMENDMENTS

Applicants did not file an Amendment After Final Rejection.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The present invention relates to a process for preparing optically active hydroxy-, alkoxy-, amino-, alkyl-, aryl- or chlorine-substituted alcohols or hydroxy carboxylic acids having from 3 to 25 carbon atoms or their acid derivatives or cyclization products by hydrogenating the correspondingly substituted optically active mono- or dicarboxylic acids or their acid derivatives. See page 1, lines 5-9, of Applicants' disclosure.

According to claim 1, the claimed process comprises hydrogenating a substituted optically active mono- or dicarboxylic acid or acid derivative thereof in the presence of a catalyst whose active component comprises a noble metal selected from the group consisting of Pt, Pd, Rh, Ir, Ag, and Au and at least one further element selected from the group consisting of Sn, Ge, Mo, W, Ti, Zr, V, Mn, Fe, Co, Ni, Cu, Zn, Ga, In, Pb, Bi, Cr, Ce, Pr, Nd, Pm, Sm, Eu, Gd, Tb, Dy, Ho, Er, Tm, Yb, and Lu. See page 2, lines 25-33, of Applicants' disclosure.

According to claim 2, the claimed process comprises a noble metal selected from the group consisting of Pt, Pd, Rh and Ir. See page 9, lines 23-26, of Applicants' disclosure.

According to claim 3, the claimed process comprises at least one further element being selected from the group consisting of Sn, Ge, Cr, Mo and W. See page 9, lines 17-18, of Applicants' disclosure.

According to claim 4, the claimed process comprises that the at least one further element is Sn. See page 9, lines 17-18, of Applicants' disclosure.

According to claim 5, the claimed process comprises that the active component of the catalyst comprises Pt and Sn. See page 9, lines 25-26, of Applicants' disclosure.

According to claim 7, the claimed process comprises that the hydrogenation results in a product selected from the group consisting of 1,2-propanediol, 1,2-butanediol, 1,2-pentanediol, 1,3-pentanediol, leucinol, isoserinol, valinol, isoleucinol, serinol, threoninol, lysinol,

phenylalaninol, tyrosinol, prolinol, 2-chloropropanol, 2-methyl-1-butanol, 2,3-dimethylbutane-1,4-diol, 2-methylbutane-1,4-diol, 1,2,4-butanetriol, 1,2,5-pentanetriol, 1,2,6-hexanetriol, 2-hydroxy- γ -butyrolactone, 3-hydroxy- γ -butyrolactone, 2-chloro- γ -butyrolactone, 3-chloro- γ -butyrolactone, 2-amino- γ -butyrolactone, 3-amino- γ -butyrolactone, 2-methyl- γ -butyrolactone, 3-methyl- γ -butyrolactone, 3-hydroxy- δ -valerolactone, 4-hydroxy- δ -valerolactone, 2-hydroxytetrahydrofuran, 2-methyltetrahydrofuran, 2-aminotetrahydrofuran, and 3,4-dihydroxybutyric acid. See page 8, line 4 to page 9, line 6, of Applicants' disclosure.

According to claim 8, the claimed process comprises that the catalyst is a supported catalyst. See page 9, lines 28-33, of Applicants' disclosure.

According to claim 9, the claimed process comprises that the catalyst, based on the total weight of the catalyst and calculated as the metal, comprises from 0.01 to 30% by weight of the noble metal and from 0.01 to 50% by weight of the at least one further element. See page 10, lines 15-19, of Applicants' disclosure.

According to claim 10, the claimed process comprises that the support material is selected from ZrO_2 , TiO_2 , Al_2O_3 , SiO_2 , activated carbon, carbon blacks, graphites or high-surface area graphites. See page 9, line 42 to page 10, line 4, of Applicants' disclosure.

According to claim 11, the claimed process comprises that the noble metal and the at least one further element are applied to the support in the presence of a reducing agent. See page 12, lines 1-2, of Applicants' disclosure.

According to claim 12, the claimed process comprises that the hydrogenation is conducted at a pressure of from 100 to 300 bar. See page 12, line 30, of Applicants' disclosure.

According to claim 13, the claimed process comprises that the hydrogenation is conducted at a temperature of from 30 to 180°C. See page 12, lines 27-28, Applicants' disclosure.

According to claim 14, the claimed process comprises that the hydrogenation is conducted in the presence of an acid. See page 12, line 39, of Applicants' disclosure.

According to claim 15, the claimed process comprises that the at least one further element is selected from the group consisting of: Sn, Ge, Cr, Mo and W. See page 10, line 40, of Applicants' disclosure.

According to claim 16, the claimed process according to claim 2, comprises the at least one further element is Sn. See page 9, lines 17-18, of Applicants' disclosure.

According to claim 17, the claimed process comprises that the active component of the catalyst consists essentially of Pt and Sn. See page 9, lines 25-26, of Applicants' disclosure.

According to claim 18, the claimed process comprises that the substituted optically active mono- or dicarboxylic acid or acid derivative thereof has at least one stereocenter in the α - or β -position to at least one carboxylic acid function or acid derivative function to be hydrogenated. See page 3, lines 22-26, of Applicants' disclosure.

According to claim 19, the claimed process comprises that the support material is selected from ZrO_2 , TiO_2 , Al_2O_3 , SiO_2 , activated carbon, carbon blacks, graphites or high-surface area graphites. See page 9, line 42 to page 10, line 4, of Applicants' disclosure.

According to claim 20, the claimed process comprises that the hydrogenation is conducted in the presence of a reducing agent, an acid or a reducing agent and an acid. See page 12, lines 1-2, of Applicants' disclosure.

According to claim 21, the claimed process comprises that the active component of the catalyst consists essentially of Pt and Sn. See page 9, lines 25-26, of Applicants' disclosure.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

A. Has the Examiner established that claims 1, 2, 8, 10, 12-14, and 18 are not patentably distinct from claims 1, 5, 6, 9, and 12-17 of U.S. Patent No. 7,507,866 to Urtel et al. and that the claims are, therefore, unpatentable on the grounds of nonstatutory obviousness-type double patenting?

B. Has the Examiner established that claims 1-5 and 7-21 are obvious over U.S. Patent No. 4,985,572 to Kitson (hereinafter “Kitson”) in view of U.S. Patent No. 5,731,479 to Antons (hereinafter “Antons”) and that the claims are, therefore, unpatentable under 35 U.S.C. §103(a)?

VII. ARGUMENT

A. The nonstatutory obviousness-type double patenting rejection has been overcome by the filing of a terminal disclaimer.

The rejection of claims 1, 2, 8, 10, 12-14, and 18 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 5, 6, 9, and 12-17 of U.S. Patent No. 7,507,866 to Urtel et al. has been overcome by the concurrent filing of a Terminal Disclaimer. The filing of the Terminal Disclaimer is not to be construed as an admission, estoppel or acquiescence. See *Quad Environmental Technology v. Union Sanitary District*, 20 USPQ2d 1392 (Fed. Cir. 1991) and *Ortho Pharmaceuticals Corp. v. Smith*, 22 USPQ2d 1119 (Fed. Cir. 1992).

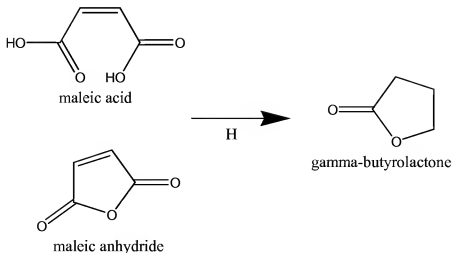
B. Kitson and Antons do not render obvious claims 1-5 and 7-21 because the Examiner has ignored the fact that Antons teaches away from the proposed combination of references.

Claims 1-5 and 7-21 have been rejected under 35 U.S.C. §103(a) as being unpatentable over US Patent No. 4,985,572 to Kitson et al. in view of US Patent No. 5,731,479 to Antons.

Claim 1 recites, among other features, a process for preparing optically active hydroxy-, alkoxy-, amino-, alkyl-, aryl- or chlorine-substituted alcohols or hydroxy carboxylic acids having from 3 to 25 carbon atoms or their acid derivatives or cyclization products. Claim 18 recites, among other features, a process for preparing optically active compounds, the process comprising hydrogenating a substituted optically active mono- or dicarboxylic acid or corresponding acid derivative thereof. At least these features of the independent claims cannot reasonably be considered to be suggested in Kitson.

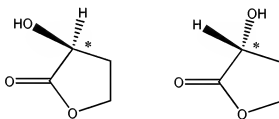
As appreciated by the Examiner, Kitson does not teach that the process therein can be used for the production of optically active compounds. However, the April 2, 2009 Office Action asserts, at page 6, lines 15-16, that Kitson teaches that all derivatives of carboxylic acids, including optically active carboxylic acids, may be used. As best understood by Applicants, the Office Action asserts that the catalyst in Kitson is considered to be able to reduce any carboxylic acid to the corresponding alcohol. The alcohols obtained in Kitson are, however, not optically active.

The April 2 Office Action further asserts, at page 7, line 7, that Kitson suggests, at col. 6, line 38, compounds exhibiting a stereocenter. This assertion is wrong. Kitson teaches, at col. 6, lines 38 -39, the hydrogenation of malaic [sic] acid or maleic anhydride to gamma-butyrolacton, i.e., the following reaction:



Neither the reactants, maleic acid or maleic anhydride, nor the product, gamma-butyrolactone, have a stereocenter. These three compounds are, therefore, not optically active. Accordingly, Kitson fails to suggest producing optically active compounds, as claimed.

A stereocenter in a chemical compound may be carbon atom carrying four different substituents. One example is 2-hydroxy- γ -butyrolactone having one stereocenter, indicated by an asterisk, the two enantiomers of which are shown below:



In this context, Applicants respectfully disagree with the assertion in the October 26, 2009 Advisory Action at paragraph 3, line 8, that claim 7 of this application recites gamma-butyrolactone [sic]. Gamma-butyrolactone is not an optically active compound and can, thus, not be the desired reaction product of a process for preparing optically active compounds. Claim 7 recites, however, optically active derivatives of gamma-butyrolactone, such as the above-noted 2-hydroxy- γ -butyrolactone.

Moreover, Applicants note that the Advisory Action merely repeats the factually wrong statement of the April 2 Office Action at page 9 that gamma-butyrolactone is optically active. In the same paragraph, the Office Action also characterized tetrahydrofuran as being an alcohol. It is not. Tetrahydrofuran is a cyclic ether. Even more troubling than the perceived carelessness in assessing Applicants' arguments is the impression that the repeated mischaracterization of gamma-butyrolactone as an optical active compound stems from an underlying lack of familiarity with the concept of optically active compounds.

Antons teaches, at col. 1, lines 27-30, that certain catalytic reductions of carboxylic acids to alcohols cannot be performed with optically active reagents because the reaction leads to racemization, i.e., to a non-optically active product containing both enantiomers. In the parlance

of the Office Action, Antons teaches at the above passage that optically active reactants can be reduced. However, a reduction resulting in racemization cannot reasonably be considered to suggest a process for preparing optically active hydroxy-, alkoxy-, amino-, alkyl-, aryl- or chlorine-substituted alcohols or hydroxy carboxylic acids, as recited in claim 1, or a process for preparing optically active compounds, as recited in claim 18. It is, of course, not the issue if optically active reactants may be reduced by the method of Kitson, but if the method in Kitson would yield optically active alcohols. A skilled artisan, having Kitson and Antons available to her, would have no reasonable expectation that using the optically active reagents of Antons with the catalysts of Kitson would produce optically active products because Antons teaches away from the proposed combination of citations in the Office Action.

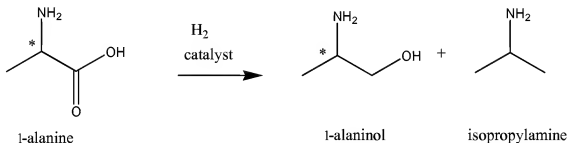
Antons teaches, at col. 1, lines 34-38, a process for the preparation of optically active alcohols, wherein optically active carboxylic acids are reduced with hydrogen at temperatures below 160 °C and pressures below 250 bar, in the presence of ruthenium catalysts. Throughout the entire disclosure of Antons, a skilled artisan is apprised that varying the reaction conditions, such as increasing the temperature, increasing the pressure, or switching the catalyst, leads to racemization, i.e., to the production of a non-optically active product. For example, at col. 4, lines 61-67, Antons teaches that using copper chromite catalysts leads to the production of propane-1,2-diol that was extensively racemized and the formation of other reaction products. Moreover, Antons teaches, at col. 5, lines 1-5, that the use of Raney nickel, a catalyst well known for the reduction of carboxylic acid esters to alcohols, dissolves partially and that no propane-1,2-diol can be isolated from the reaction mixture.

In other words, Antons teaches a process for preparing optically active alcohols using ruthenium catalysts. Antons teaches away from switching to a different catalyst because catalysts other than ruthenium may produce a racemate or may not even catalyze the reduction to the intended product. The Advisory Action states, at paragraph 3, that Antons does not teach away from using the catalyst. The Advisory Action, however, fails to provide any reasoning for this assessment. As such, the Advisory Action failed to meet its burden answering the substance of Applicants' arguments, as set forth in MPEP 707.07(f).

Moreover, the Advisory Action states that Applicants' other arguments are irrelevant to the claims. While it is unclear to which arguments the Advisory Action refers, Applicants note that the October 2, 2009 Amendment argued that the claimed method achieves unexpected results, which are evidence of non-obviousness. By failing to evaluate Applicants' rebuttal arguments, the Advisory Action fails to comply with its burden of answering all asserted advantages, as further set forth in MPEP 707.07(f). In addition, it remains a mystery as to why evidence of non-obviousness would be irrelevant to the claims.

In particular, as previously noted, even if Antons and Kitson would have been combined in the manner suggested in the April 2 Office Action, a skilled artisan would not have expected the remarkably low formation of isopropylamine as a side product, which is achieved by the claimed process. In particular, Applicants compared the ruthenium catalyst disclosed in Antons for the hydrogenation of optically active carboxylic acids, using the example of L-alanine, with a Pt/Sn-on carbon black catalyst as claimed.

Specifically, the following hydrogenation reaction of L-alanine to L-alaninol was monitored for both catalysts and the formation of the undesired side-products isopropylamine measured:



The hydrogenation of L-alanine, as shown above, was carried out in the presence of i) Ru-black, the catalyst according to Antons, and ii) on Pt/Sn-on-carbon, which is a preferred embodiment of the claimed subject matter. Hydrogenation took place under identical reaction conditions, which are the same as example 2 of Applicants' disclosure. Specifically,

hydrogenation was performed in a stainless steel autoclave at 100 °C at a hydrogen pressure of 200 bar.

The results after a hydrogenation time of 12 hours are summarized in the following table. After converting more than 99% of L-alanin to L-alaninol, no decarbonylation side reaction could be detected with the Pt/Sn-on-carbon catalyst.

Catalyst	L-alanine (wt.-%)	L-alaninol	Conversion of L-alanine (%)	Isopropylamine (wt.-%)	Selectivity of iso- propylamine (%)	Selectivity of alaninol (%)
Ru-black	<0.005	2.0	> 99	0.07	0.6	13.5
Pt/Sn-on- carbon	< 0.005	3.6	> 99	< 0.005	0.0	24.3

Remarkably and unexpectedly, the claimed process reduces the unwanted formation of isopropylamine to under 0.005 wt.-%.

Applicants have presented the above experimental data already in the response to the previous Office Action filed January 15, 2009. The April 2 Office Action and the Advisory Action fail to acknowledge that Applicants supplied this data, let alone comment on the persuasiveness of the data supplied.

Claims 2-5, 7-17, and 19-21 are in condition for allowance for at least their respective dependence on allowable claims 1 and 18, as well as for the separately patentable subject matter that each of claims 2-5, 7-17, and 19-21 recite.

VIII. CLAIMS

A copy of the claims involved in the present appeal is attached hereto as Appendix A.

Applicants concurrently herewith submit the requisite fee for the filing of an Appeal Brief. Applicants believe no additional fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 22-0185, under Order No. 12810-00340-US1 from which the undersigned is authorized to draw.

Dated: November 30, 2009

Respectfully submitted,

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APPENDIX A – CLAIMS ON APPEAL**Claims Involved in the Appeal of Application Serial No. 10/588,948**

1. A process for preparing optically active hydroxy-, alkoxy-, amino-, alkyl-, aryl- or chlorine-substituted alcohols or hydroxy carboxylic acids having from 3 to 25 carbon atoms or their acid derivatives or cyclization products, the process comprising hydrogenating a substituted optically active mono- or dicarboxylic acid or acid derivative thereof in the presence of a catalyst whose active component comprises a noble metal selected from the group consisting of Pt, Pd, Rh, Ir, Ag, and Au and at least one further element selected from the group consisting of Sn, Ge, Mo, W, Ti, Zr, V, Mn, Fe, Co, Ni, Cu, Zn, Ga, In, Pb, Bi, Cr, Ce, Pr, Nd, Pm, Sm, Eu, Gd, Tb, Dy, Ho, Er, Tm, Yb, and Lu,

wherein the substituted optically active mono- or dicarboxylic acid or acid derivative thereof has at least one stereocenter in the α - or β -position to at least one carboxylic acid function or acid derivative function to be hydrogenated.

2. The process according to claim 1, wherein the noble metal is selected from the group consisting of Pt, Pd, Rh and Ir.

3. The process according to claim 1, wherein the at least one further element is selected from the group consisting of Sn, Ge, Cr, Mo and W.

4. The process according to claim 1, wherein the at least one further element is Sn.

5. The process according to claim 1, wherein the active component of the catalyst comprises Pt and Sn.

6. (Canceled)

7. The process according to claim 1, wherein the hydrogenation results in a product

selected from the group consisting of 1,2-propanediol, 1,2-butanediol, 1,2-pentanediol, 1,3-pentanediol, leucinol, isoserinol, valinol, isoleucinol, serinol, threoninol, lysinol, phenylalaninol, tyrosinol, prolinol, 2-chloropropanol, 2-methyl-1-butanol, 2,3-dimethylbutane-1,4-diol, 2-methylbutane-1,4-diol, 1,2,4-butanetriol, 1,2,5-pentanetriol, 1,2,6-hexanetriol, 2-hydroxy- γ -butyrolactone, 3-hydroxy- γ -butyrolactone, 2-chloro- γ -butyrolactone, 3-chloro- γ -butyrolactone, 2-amino- γ -butyrolactone, 3-amino- γ -butyrolactone, 2-methyl- γ -butyrolactone, 3-methyl- γ -butyrolactone, 3-hydroxy- δ -valerolactone, 4-hydroxy- δ -valerolactone, 2-hydroxytetrahydrofuran, 2-methyltetrahydrofuran, 2-aminotetrahydrofuran, and 3,4-dihydroxybutyric acid.

8. The process according to claim 1, wherein the catalyst is a supported catalyst.
9. The process according to claim 8, wherein the catalyst, based on the total weight of the catalyst and calculated as the metal, comprises from 0.01 to 30% by weight of the noble metal and from 0.01 to 50% by weight of the at least one further element.
10. The process according to claim 8, wherein the support material is selected from ZrO_2 , TiO_2 , Al_2O_3 , SiO_2 , activated carbon, carbon blacks, graphites or high-surface area graphites.
11. The process according to claim 8, wherein the noble metal and the at least one further element are applied to the support in the presence of a reducing agent.
12. The process according to claim 1, wherein the hydrogenation is conducted at a pressure of from 100 to 300 bar.
13. The process according to claim 1, wherein the hydrogenation is conducted at a temperature of from 30 to 180°C.
14. The process according to claim 1, wherein the hydrogenation is conducted in the

presence of an acid.

15. The process according to claim 2, wherein the at least one further element is selected from the group consisting of: Sn, Ge, Cr, Mo and W.

16. The process according to claim 2, wherein the at least one further element is Sn.

17. The process according to claim 1, wherein the active component of the catalyst consists essentially of Pt and Sn.

18. A process for preparing optically active compounds, the process comprising hydrogenating a substituted optically active mono- or dicarboxylic acid or corresponding acid derivative thereof in the presence of a catalyst whose active component comprises a noble metal selected from the group consisting of Pt, Pd, Rh and Ir, and at least one element selected from the group consisting of Sn, Ge, Cr, Mo and W,

wherein the substituted optically active mono- or dicarboxylic acid or acid derivative thereof has at least one stereocenter in the α - or β -position to at least one carboxylic acid function or acid derivative function to be hydrogenated.

19. The process according to claim 18, wherein the catalyst is a supported catalyst, and wherein the support material is selected from ZrO₂, TiO₂, Al₂O₃, SiO₂, activated carbon, carbon blacks, graphites or high-surface area graphites.

20. The process according to claim 18, wherein the hydrogenation is conducted in the presence of a reducing agent, an acid or a reducing agent and an acid.

21. The process according to claim 18, wherein the active component of the catalyst consists essentially of Pt and Sn.

APPENDIX B - EVIDENCE

No evidence pursuant to §§ 1.130, 1.131, or 1.132 or entered by or relied upon by the examiner is being submitted.

APPENDIX C – RELATED PROCEEDINGS

No related proceedings are referenced in II. above, hence copies of decisions in related proceedings are not provided.